EDITORIAL

Illusion or reality, abstract or concrete art? Models in health: do they answer the questions?

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The Belgian surrealist artist Rene Magritte created several paintings of mundane elements, arranged to provoke a reflection on meaning. In one of his paintings he depicts an apple but just above it we read "Ceci n'est pas une pomme". In fact, it is not an apple, but the painting of an apple.

To model is to abstract, to choose the most appropriate metaphor or analogy to better understand a phenomenon[1]. Models are interfaces between humans and phenomena[2]; they are means to represent the complexity of the real world in a more simple and understandable way. Apples, whose genome was decoded only in 2010, have 17 chromosomes containing approximately 57,000 genes[3] that generate a fruit composed of approximately 85% water; 14% carbohydrates; very little protein, fiber, minerals, and vitamins; interconnected and arranged in a three-dimensional structure[4]. When we see the painting of an apple, we know it is a simplified but intelligible representation, i.e., a model of this complex fruit.

In 1972, the Nuffield Provincial Hospitals Trust, London, published a book by Archie Cochrane, "Effectiveness and efficiency: random reflections on health services", in which the author discusses the basics of what is now called evidence-based medicine, health technology assessment, and systematic review. In this book, Cochrane expressed his perception that there would never be enough monetary resources to provide all diagnostic and therapeutic procedures that doctors can invent, and therefore, it is imperative to test and validate how we invest those resources, derived from public or private funds, to ensure reduced morbidity and/or mortality[5].

In the last four decades, more intensely in the last twenty years, as a result of Cochrane's ideas, the healthcare professionals' community learned how to use and became accustomed to the format, language, and specific aspects (statistical and epidemiological) of the two main models that are used in our area of knowledge: clinical trials and systematic reviews/meta-analyses.

Clinical trials are models of more complex situations faced in everyday life[6,7] and meta-analyses are models to help us understand the overall results of several clinical trials performed to answer the same specific clinical question. We all strive to better and more properly interpret the results of these models, so that we can use them in our daily clinical practice.

Indeed, the last two decades have been very fruitful in developing new diagnostic and therapeutic technologies that are often more effective than those existing but that are also more expensive, as envisioned by Cochrane. The world has witnessed rapid growth in healthcare costs, a problem that plagues low, middle, and high-income countries[8].

Brazil is no exception. Hence, aiming to regulate, to streamline, and to rationalize the process of incorporating health technologies, in accordance with social needs and SUS (Sistema Único de Saúde - Unified Health System) management, Law 12,401 of April 28th, 2011 was passed. Resulting from a legislative movement to rationalize the incorporation of healthcare technologies originated at the beginning of the last decade, the law requires that in order to incorporate a particular technology into the SUS it is necessary to prove its cost-effectiveness and demonstrate its budget impact[9].

The proposition of Law 12,401 is fully in line with Cochrane's thought who forty years ago said that "If we are ever going to get the 'optimum' results from our national expenditure on the National Health Service (NHS) we must finally be able to express the results in the form of the benefit and the cost to the population of a particular type of activity, and the increased benefit that could be obtained if more money were made available."[5].

Given the rising costs and limited resources of global and national healthcare systems, and the very existence of the Law 12,401, we will more frequently find articles presenting a pharmacoeconomic evaluation of a medical technology in international and Brazilian medical journals. These assessments are called pharmacoeconomic because they take into account not only clinical outcomes or consequences but also the cost of a given health technology, as proposed by Cochrane.

Pharmacoeconomic evaluations may be based on the so-called pharmacoeconomic models, which are an analytical methodology that considers the occurrence of events over time and across populations based on data obtained from primary or secondary sources, whose purpose is to estimate the effects of an intervention in terms of health consequences and costs. They are models that help us determine the efficiency of a healthcare technology[7].

Thus, to understand the healthcare setting reality in which financial resources are limited, and whose proper allocation is of paramount importance to maximize health with the available resources, we have to strive to understand and interpret these new pharmacoeconomic models, which take into account the clinical and economic aspects of the incorporation of a technology into the healthcare system[8].

In this issue of RAMB, Nita ME et al.[10] present the results of a pharmacoeconomic model which assesses the cost-effectiveness of saxagliptin added to metformin for the treatment of type 2 diabetes mellitus in the Brazilian private healthcare setting. To critically appraise a pharmacoeconomic study, Michael Drummond[11,12] suggests that we analyze ten points:

1. Was a well-defined question structured in an answerable form?
2. Was a comprehensive description of the competing alternatives provided?
3. Are there evidences that the effectiveness of the program/technology has been established?
4. Were all the important and relevant costs and clinical outcomes identified for each competing alternative?
5. Were costs and clinical outcomes measured accurately and in appropriate units?
6. Were costs and outcomes evaluated credibly?
7. Were costs and clinical outcomes adjusted for the time of their occurrence (discount)?
8. Was an incremental costs and outcomes analysis (clinical consequences) of the competing alternatives accomplished?
9. Was uncertainty taken into account in the estimates of costs and consequences?
10. Did the presentation and discussion of study results comprise all topics of concern to users?

For the study of Nita ME et al.[10] the answer to most of these questions is yes. But as with any model, we can always deepen the discussion.

In this case, from the medical point of view, we should consider the fact that the patients included in the model are those who failed to achieve the glycemic control goals. Glycemic control, in turn, is affected by adherence to treatment, such that[13] regimens where the drug is taken once a day have higher rates of adherence than regimens where the medicine is taken twice a day[14], and monotherapy regimens demonstrate higher adherence rates than polytherapy regimens[15].

What is proposed in this pharmacoeconomic study is the addition of another drug to the therapeutic scheme; but adherence to treatment is not considered in the model. Still, in relation to better glycemic control and adherence to therapy, we should consider that other interventions can improve adherence to treatment[16] and to the system of self-management, reducing mortality and disability, improving the quality of life[17-19] without adding a new drug to the regimen.

Additionally, despite the fact that the model being presented is based on the United Kingdom Prospective Diabetes Study (UKPDS) model, one of the best to predict long-term outcomes in patients with diabetes, the latter does not include among the complications the occurrence of diabetic neuropathy, which is a well-known cause of morbidity, such as lower limb amputation, and reduced quality of life[20], parameters that, if considered, probably would have changed the model's clinical and economic results.

It is important to note that changing both clinical and economic outcomes does not necessarily imply that the final conclusion of the study/model would be different. Moreover, from the modeling point of view, as the presented model is based on the UKPDS, the risk equations are those found for the British population and not yet validated for the Brazilian population.

Thus, the need for external validation of the model presented in this issue of RAMB becomes more important, and it can be accomplished by comparing the results projected in the study, for example, with external epidemiological data not used in this evaluation[21]. A good agreement between the predictions of the simulation and the external data would help validate the accuracy of the model, and it would be important to infer whether it may or may not represent the population being simulated.

Finally, the economic evaluation for reimbursement of medicines and other healthcare technologies is mandatory in many countries, including Brazil. Hence, pharmacoeconomics, with its techniques and models, is here to stay.

As we have seen, there are several challenges to overcome, mainly related to methodological issues, which, in turn, leads us to a more careful analysis and interpretation of results, because, after all, as Magritte pointed out, every time we see an apple painting, we should remember that this model gives us the illusion that we interpret to be "an apple." But what apple? The technological apple? The sin apple? Or, simply, the fruit?

But whatever the apple, there will always be more than one picture to represent it.

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